PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/008587	30.07.2004	31.07.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/165, A61K47/32, A61K47/38

Applicant
CALLUNA PHARMA BVBA

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/008587

IAP5 Rec'd PCT/PTO 30 JAN 2006

10/566356

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-10
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following document/s/:

   D1: EP-A-0 014 437 (SCHERING CORP) 20 August 1980 (1980-08-20)
   D2: EP-A-0 546 018 (SCHERING CORP) 16 June 1993 (1993-06-16)
   D3: WO 98/41207 A (BROWN SCOTT A ;UPJOHN CO (US)) 24 September 1998 (1998-09-24)
   D4: WO 02/41899 A (PHOENIX SCIENT INC) 30 May 2002 (2002-05-30)

2. Novelty

   D1 discloses (i) an oral suspension of florfenicol comprising purified water, propylene glycol and colloidal magnesium aluminium silicate and (ii) an injectable florfenicol solution comprising N,N-dimethylacetamide.
   The oral suspension (i) is not suitable for injection as it comprises purified water and the injectable solution (ii) is - due to the presence of N,N-dimethylacetamide - a non aqeuous solution and no aqueous suspension.

   The other documents D2-D4 disclose injectable florfenicol compositions, which differ from the subject-matter of the present application in that they do not contain water and are thus not aqueous.

   As a result, the subject-matter of claims 1-10 of the present application seems to be new in view of the cited prior art (Art. 33(2) PCT).

3. Inventive step

   The technical problem of the present application is the provision of an alternative injectable formulation of florfenicol.
   The solution of the problem by the provision of an aqueous injectable suspension is not obvious in view of the cited prior art; especially in view of D2, which states that aqueous injectable solutions of florfenicol are not practicable due to the low

solubility of florfenicol in water.
As there is no hint in any of the cited prior art documents that florfenicol, which is of low water solubility, leads to a stable suspension in water without any further addition of organic solvent, the subject-matter of the present application seems to involve an inventive step (Art. 33(3) PCT).

Re Item VIII

Certain observations on the international application

For clarity reasons of independent claim 1 the term "aqueous" should be substituted by the definition given on p.2, last but one paragraph of the description.